The Post-Polio Syndrome: Current Concepts and Treatment

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The post-polio syndrome (PPS) occurs in clinically stable individuals decades after recovery from an initial attack of paralytic poliomyelitis; it is characterized by new muscular weakness and atrophy and generalized fatigue. PPS is believed to occur when muscles originally affected by paralytic polio begin to lose their innervation and weaken as a result of the death of remaining anterior horn cells of the spinal cord. Although it has been suggested that immune dysregulation or persistence of chronic polio infection plays a role, it is more likely that motor neuron attrition is the result of metabolic dysfunction. Neurotrophic factors that enhance the stability and growth of motor neurons and their synaptic connections are being studied as a means to stall or reverse the progression of weakness and atrophy that occurs in PPS.
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The World Health Organization has set the year 2000 as the target date for the global eradication of polio.[1] Although use of the live vaccine in the Western Hemisphere continues to cause a handful of cases each year, the risk of contracting polio remains mainly through importation of the disease from areas of the world where it is endemic. Even in those areas, dramatic declines have occurred over the past 5 years. Yet the debilitation associated with polio is felt anew by some clinically stable individuals decades after their initial episode of paralytic poliomyelitis, with the onset of progressive muscular weakness known as the post-polio syndrome (PPS).

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Epidemiology of Polio

The path to the successful eradication of poliomyelitis was forged by the introduction of the inactivated polio vaccine of Salk in 1955 and the live attenuated oral polio vaccine of Sabin in 1961.[2] Since 1979, no case of paralytic poliomyelitis caused by the wild-type virus has been reported in the Western Hemisphere.[3] Throughout the world, however, poliomyelitis continues to occur due to live poliovirus and other enterovirus pathogens (coxsackievirus types A and B, echoviruses, and enterovirus types 30 and 71),[4] live vaccine,[5] infection of nonimmunized groups,[6] infection of inadequately vaccinated populations,[7] and intramuscular injections temporally related to poliovirus infection or administration of the live polio vaccine.[8]

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Development of PPS

Shortly after the development of the acute febrile illness, a small percentage of individuals infected by the poliovirus will develop varying degrees of limb and bulbar

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aralysis according to the extent of ijury and death of motor neurons. he motor neurons that survive the iitial attack of the poliovirus go n to reinnervate originally denerated muscle fibers during a peiod of recovery typically lasting ionths to years,[9] and they mainain effective neuromuscular conections with functional stability or many years.[9] Then, decades ater, some of these paralytic polio atients develop symptoms of PPS.

Although cases of patients with PS were initially described more han 100 years ago, only recently ave these new symptoms and igns been directly attributed to he paralytic disease.[10-13] While inection with the poliovirus leads to aralytic poliomyelitis in only .1% to 1% of patients,[14] more than alf of individuals who do develop aralytic poliomyelitis have been eported to have the new muscular veakness characteristic of PPS.[15-17]

Clinical Characteristics of PPS

PS comprises a constellation of ymptoms, including new muscle veakness, atrophy, and fatigue; eneralized fatigue; and muscle nd joint pain. These symptoms levelop 10 to 40 years after the inial attack of paralytic poliomyelis[13,18-22] (Table I), with the greatest ncidence occurring 30 to 40 years fter the initial infection.

Because virologic confirmation of oli infection was not available until the 1950s, older individuals describing these symptoms should provide a history of a well-documented, acute febrile illness during childhood or adolescence; preferably, this febrile illness should be associated temporally with a polio epidemic and should have resulted in partial or complete paralysis of limb or bulbar musculature (ie, of the lips, tongue, pharynx, and larynx), followed by some degree of recovery of motor function, with functional stability lasting for at least 10 years.[23] The clinical presentation of residual muscle atrophy, weakness, and areflexia in at least 1 limb with normal sensation, accompanied by histopathologic and electromyographic findings of chronic denervation, support the diagnosis of previous paralytic poliomyelitis. Within this clinical setting, presentation of newly progressive weakness, atrophy, muscle or joint pain, and fatigue suggests the diagnosis of PPS. However, the clinician must exclude other known medical, neurologic, orthopedic, and psychiatric disorders that may help to explain the development of the patient's new symptoms, such as back injuries, radiculopathies, compression neuropathies, degenerative arthritis, hyper- or hypothyroidism, fibromyalgia, anxiety, and depression.

Table I
Clinical Features of Post-Polio Syndrome

Neuromuscular
PPMA (new weakness of appendicular, bulbar, or respiratory muscles; new muscular atrophy; myalgias; fasciculations)
Muscle fatigue
New respiratory difficulties
Sleep apnea
Musculoskeletal
Joint pain
Joint and skeletal deformities
Decreased endurance
General
Generalized fatigue
Intolerance to cold
Increased sleep requirements
Psychologic problems

PPMA = post-polio muscular atrophy.

Post-Polio Muscular Atrophy

Of all of the individuals diagnosed with poliomyelitis, only a small percentage of patients actually develop new symptoms of slowly progressive muscle weakness and atrophy, with or without fatigue, after many years of functional stability.[15-18,22,24,25] These symptoms are attributable to post-polio progressive muscular atrophy (PPMA), the further deterioration of remaining motor neurons and their collateral neuromuscular connections. The new weakness is usually randomly distributed and asymmetric, and it may involve portions of 1 or more muscles of any limb. Although it appears that any muscle is ultimately vulnerable, including those without previous clinical involvement, muscles previously affected by the original attack of polio, whether fully or partially recovered, are more likely to become involved than muscles that were clinically unaffected by the original infection.[26] As the remaining previously stable muscles become progressively weaker, daily activities—which, for many years after recovery from acute paralytic poliomyelitis, may have been accomplished by remarkable compensatory improvisation—become increasingly more difficult to perform. In some of these patients, intrinsic muscle pain, cramps, and coarse fasciculations—indications of an ongoing neurogenic process—may either precede or be associated with the new muscle weakness.[19,25,27]

Dysphagia. In addition to involvement of appendicular muscles, new weakness of bulbar muscles may develop in patients with PPMA.[28,29] Although only 10% to 20% of polio patients actually complain of residual dysphagia, it appears that nearly all individuals with PPMA evaluated with videofluoroscopy demonstrate asymmetric weakness of pharyngeal or laryngeal muscles; impaired tongue movements; pooling in the valleculae or pyriform sinuses; or, rarely, aspiration.[30] Patients commonly complain of food or pills sticking in the throat, and intermittent choking on food. When present, symptoms of dysphagia are progressive and more severe in patients who have had

previous clinical bulbar involvement, although subclinical dysfunction may be detected in bulbar muscles clinically spared by the initial illness.[29]

Respiratory symptoms. Progressive respiratory insufficiency is seen in patients left with diminished respiratory reserve after the acute attack of polio.[31,32] In most cases, patients functioning with marginal respiratory capacity (eg, those who become easily tired or short of breath on exertion), who may have been weaned successfully from ventilator use after recovery from the acute illness, ultimately develop progressive respiratory difficulties.[32] Respiratory insufficiency directly related to PPMA is usually caused by residual diaphragmatic muscle weakness, or, more rarely, occurs as a result of central hypoventilation from bulbar involvement of the reticular activating system (a network of neurons in the spinal cord, brain stem, and thalamus that controls many unconscious motor activities) and sleep regulatory centers. Secondary causes also may contribute, including progressive scoliosis, pulmonary emphysema, cardiovascular insufficiency, and inactivity.[33]

Sleep apnea is often found in PPMA patients in association with other symptoms of respiratory compromise and residual bulbar dysfunction.[32,34,35] The central component of this common problem is dysfunction of the reticular formation. Peripheral factors include progressive weakness of diaphragmatic, intercostal, abdominal, and pharyngeal muscles; obesity; emphysema; and musculoskeletal deformities.

Fatigue. The majority of patients with PPS, and nearly all patients with PPMA, experience fatigue and diminished stamina. Patients may describe a generalized, overpowering feeling of tiredness and malaise unrelated to physical activity, or may feel a more specific sensation of fatigue localized to muscles. In contrast to patients with multiple sclerosis (MS) or chronic fatigue syndrome (CFS), who frequently experience a generalized malaise throughout the day, PPS patients usually develop midday fatigue that is ameliorated by brief rest periods. Psychopathologic symptoms of anxiety, depression, and stress are not cofactors in the development of fatigue in patients with PPS.[36]

Many survivors of paralytic poliomyelitis develop new musculoskeletal symptoms,[15,22,37-40] including diminished functional aerobic capacity, decreased endurance, and weight gain; these symptoms are combined with degenerative arthritis, scoliosis, and pain in joints that have been biomechanically disadvantaged or deformed owing to long-standing asymmetry of size and strength of previously affected muscles. Although these new musculoskeletal deficits are often a prominent feature of PPS, there is no evidence that they represent neuromuscular sequelae of prior polio. Rather, these new symptoms are invariably the result of secondary processes such as long-standing scoliosis, obesity, and childhood surgical interventions. The latter—including tendon transfers, joint fusions, and shortening of the long bones of the lower extremities[40] intended to improve mobility and stability after recovery from the acute paralytic illness—may unpredictably alter the natural biomechanics of joints during subsequent growth and recovery from paralysis, resulting in excessive wear and tear on joints, ligaments, and tendons. New musculoskeletal complaints in patients with prior paralytic poliomyelitis, directly or indirectly attributable to prior polio, should be considered as elements of PPS, although they are not neuromuscular in origin (Table I).

Childhood surgical intervention—including tendon transfers, joint functions, and shortening of the long bones of the lower extremities—may unpredictably alter the natural biomechanics of joints during subsequent growth and recovery from paralysis.

Epidemiology of PPS

There are more than 1.63 million survivors of paralytic poliomyelitis.[23] Between 20% and 60% of these individuals may develop PPS,[15,23,41] but when individuals with musculoskeletal symptoms are excluded, the percentage of paralytic poliomyelitis patients who develop PPMA appears to be much lower.[10,42] Individuals more likely to develop PPS include older patients[15,43] who have tended to develop more severe weakness during the acute paralytic illness[34,41] and have experienced greater residual deficits,[26] as well as those presenting after longer periods of stability.[43] The interval of clinical stability ranges from 8 to 71 years,[18] with the highest incidence of PPS occurring 30 to 40 years after the acute polio attack.[18,19,34]

The natural course of the symptoms of fatigue and pain of PPS is difficult to assess because these complaints are not amenable to objective assessment. On the other hand, the power of muscles weakened by PPMA may be quantified, and it appears to diminish at a variable but slow rate of about 1% per year,[25] although the patient may experience periods of relative stability lasting many years.[42,44,45] Slowly progressive loss of strength of the tongue and swallowing muscles appears to occur more consistently.[24]

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Pathogenesis of PPMA. The cause of new anterior horn-cell degeneration and denervation in muscles of patients with PPMA is unknown. The development of PPMA in younger patients cannot be explained by aging, which normally leads to gradual motor-neuronal loss only in individuals above the age of 60.[46] More likely, after many years of stability, the chronically increased metabolic burden placed on the neuron becomes too great to sustain all of its synapses, leading to a slow attrition of sprouts and the ultimate death of the motor neuron.[18,47] However, recent studies have raised the possibility that immune dysregulation or persistence of chronic polio infection may be responsible for new neuromuscular symptoms.

During the initial paralytic attack by the poliovirus, muscles are weakened to varying degrees, depending on the extent of injury or death of anterior horn cells of the spinal cord.[48,49] Whether muscles recover partially or completely depends on the ability of injured, healing motor neurons and normal, unaffected neurons to generate distal axonal sprouts to neighboring muscle fibers that have lost their innervation.[50-52]

Neuronal findings. Electrophysiologic recordings demonstrate abnormally large motor units of prolonged duration, both in weakened and clinically uninvolved muscles of polio patients, as remaining motor neurons reinnervate up to 5 times their normal complement of muscle fibers.[26,50-54] During a prolonged period of relative stability, new axonal sprouting occurs in previously uninvolved or recovered neurons as other motor neurons that can no longer sustain the increased numbers of connections begin to die.[32] Electrical studies of individual fibers innervated by a single motor axon in muscle of patients with either stable polio or PPMA demonstrate a high variability of impulse conduction (jitter), which continues indefinitely.[51-53,55] Jitter is not seen in normally innervated motor units and suggests the presence of ongoing denervation. Nerve cell adhesion molecules (N-CAMs), expressed on the surface of muscle fibers only after they lose innervation, are present in both stable and weakening post-poliomyelitis muscles,[52,56] providing a histologic correlate of remodeling of the motor unit. New muscle weakness and atrophy occur when the attrition of these neurons outweighs the capacity of the remaining anterior horn cells to sprout and innervate newly denervated muscle fibers, which is reflected histologically by increasing numbers of N-CAM–positive, denervated muscle fibers (Fig. 1).

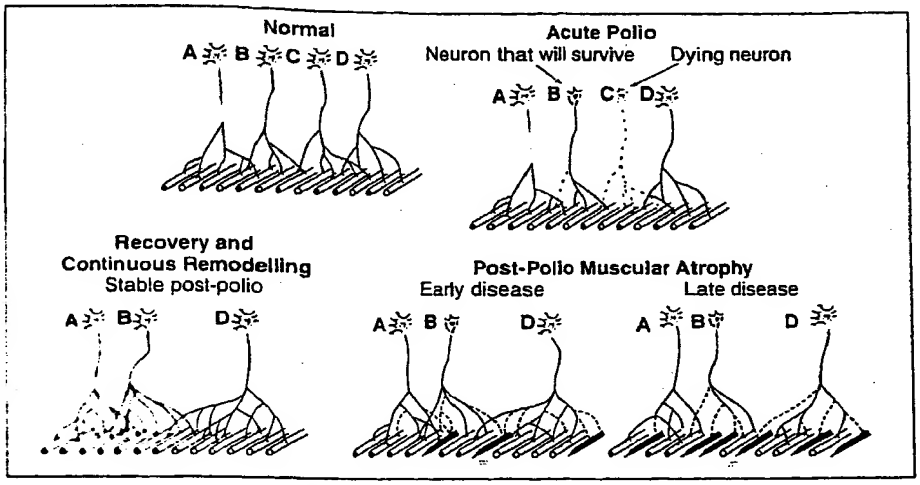

Figure 1. Remodelling of motor units during acute polio and early and late post-polio muscular atrophy: PPMA. Under normal conditions, anterior horn cells innervate set complement of muscle fibers in striated muscle. Acute paralytic poliomyelitis leads to injury or death of some of these cells. Remodeling of remaining motor neurons occurs during stable post-polio with effective reinnervation of newly denervated muscle fibers. Greater numbers of muscle fibers become denervated with progression of PPMA, resulting in presence of denervated atrophic muscle fibers in groups. Adapted from Advances in Neurology: Amyotrophic Lateral Sclerosis (1991; p 506), Copyright © 1991, Lippincott-Raven Healthcare.[33]

Immunologic findings. Immunologic abnormalities have been observed in a fraction of patients with PPMA, including mild inflammation consisting of CD8+ and CD4+ cells surrounding healthy muscle fibers that express MHC class I antigens on their surface; this inflammation is similar to that seen in immune-mediated myopathies,[57] inflammation in the parenchyma of gray matter of spinal cord,[58,59] intrathecal oligoclonal IgG bands,[24] and activated T cells in peripheral blood.[60] It has been suggested that immunologic dysregulation may play a role in the development of new symptoms of weakness and atrophy due to motor neuron degeneration,[24,34,56] although direct evidence for this theory is not yet forthcoming.

Although poliovirus is lytic and produces a monophasic illness,[4] an intriguing proposed hypothesis postulates that defective poliovirus particles or mutant viruses, having escaped detection by the immune system by persisting indefinitely in motor neurons that did not lyse, are subsequently reactivated to cause the death of these cells.[56,61,62] This hypothesis has been supported by the presence of intrathecal poliovirus-specific IgM and IgG antibodies, and high IgM antibody titers to

Table II
Differential Diagnoses

Degenerative arthritis: Patients develop joint pain, without muscle atrophy or fasciculations; serum muscle enzymes are normal; electrodiagnostic and muscle biopsy studies do not demonstrate features of denervation.
Fibromyalgia: Patients experience generalized muscle soreness, fatigue, and malaise in the absence of clinical evidence of muscle atrophy or fasciculations, elevation in serum muscle enzymes, and normal electrodiagnostic and muscle biopsy evaluations.
Radiculopathy: Patients experience new signs of asymmetric muscle weakness, atrophy, and fasciculations. Associated symptoms of pain and paresthesias are not typically experienced by post-polio syndrome (PPS) patients. Neuroimaging of cervical or lumbar spine excludes degenerative disc disease or spinal stenosis.
Multiple sclerosis (MS) or chronic fatigue syndrome (CFS) as causes of fatigue: MS or CFS patients frequently experience malaise throughout the day; PPS patients usually develop midday fatigue ameliorated by brief periods of rest. MS is accurately diagnosed by typical central nervous system MRI and cerebrospinal fluid studies. In contrast to patients with PPS, patients with electrodiagnostic evaluations are typically normal in patients with CFS. Psychopathologic symptoms of anxiety, depression, and stress are not cofactors in the development of fatigue in patients with PPS, as they may be in patients with MS and CFS.
Compression peripheral neuropathies: Impingement of peripheral nerves of upper or lower extremities, resulting from long-standing musculoskeletal deformities or other unrelated processes, leads to asymmetric muscle atrophy. Pain and paresthesias are usually associated symptoms. Electrodiagnostic testing differentiates these peripheral neurogenic processes from the motor neuron disjunction of PPS.
Acquired primary myopathy (eg, inclusion-body myositis [IBM]): Like PPS, IBM advances slowly and asymmetrically, and there may be electromyographic abnormalities resulting from secondary distal axonal degeneration. PPS is excluded by muscle biopsy demonstrating typical inflammatory and structural histopathologic features of IBM (eg, rimmed vacuoles, endomysial inflammation, variable fiber size, and eosinophilic cytoplasmic inclusions).
Amyotrophic lateral sclerosis (ALS): ALS begins focally but progresses diffusely to involve bulbar and respiratory muscles, nearly always producing hyperreflexia, spasticity, and plantar extensor responses. These upper motor neuronal signs are only rarely discovered in PPS.
Progressive muscular atrophy (a variant of ALS): Consider whether there is a lack of upper motor neuronal involvement. Distinguished from PPS by rapid progression of atrophy. Occasionally, distinction may be made by muscle biopsy, which may reveal abnormally large fiber-type grouping in PPS.
Multifocal motor neuropathy disease of peripheral nerves: Slowly progressive asymmetric weakness and atrophy develop without changes in sensation. PPS is excluded by presence of characteristic electrodiagnostic nerve conduction abnormalities and demonstration of high titers of antiganglioside antibodies in the blood.

nosis of PPS is not difficult in an individual with a previously documented history of paralytic poliomyelitis who subsequently develops new musculoskeletal symptoms, signs, and weakness, and in whom other neurologic, orthopedic, and medical disorders have been excluded—these include radiculopathies, compression neuropathies, myopathy, fibromyalgia, and arthritis (Table II). For patients in whom the diagnosis of paralytic poliomyelitis is questionable, electrodiagnostic and histopathologic indications provide evidence of previous paralytic poliomyelitis.

On occasion, however, other neuromuscular processes must be considered when a well-documented history of polio is not forthcoming or when the pace of neuromuscular deterioration is rapid. For example, amyotrophic lateral sclerosis (ALS), a relatively rapidly progressing fatal disease of the motor neurons, may begin focally, but it progresses diffusely to involve bulbar and respiratory muscles and nearly always produces hyperreflexia, spasticity, and plantar extensor responses—upper motor neuronal signs that rarely are found in PPS.[18] In the absence of upper motor neuronal involvement, the clinician should consider progressive muscular atrophy, a variant of ALS that may be distinguished from PPS only by the rapid progression of that disease. PPS may sometimes be confused with multifocal motor neuropathy,[73,74] a disease of the peripheral nerves in which slowly progressive asymmetric weakness and atrophy develop without changes in sensation. However, the presence of characteristic electrodiagnostic nerve conduction abnormalities[73,74] and the demonstration of high titers of antiganglioside antibodies in the blood[75,76] of these patients exclude PPS.

On rare occasions, an individual diagnosed initially as having PPS actually may have been weakened by a long-standing acquired primary myopathy such as inclusion-body myositis,[57,77] which also advances slowly in an asymmetric manner and which may display neurogenic electromyographic features because of secondary distal axonal degeneration.[78,79] A muscle biopsy demonstrating typical inflammatory and structural histopathologic features specific for inclusion-body myositis (eg, rimmed vacuoles, endomysial inflammation, variable fiber size, and eosinophilic cytoplasmic inclusions) will confirm the diagnosis of this myopathy.[77]

Treatment

Management of PPS addresses several aspects of the syndrome: muscular weakness, general fatigue, cardiovascular and respiratory

poliovirus in serum of a small number of patients with PPMA, suggesting a new immune response against poliovirus.[63-65] Further, amplification of poliovirus RNA particles from spinal fluid by polymerase chain reaction has revealed incomplete polioviral and other enteroviral sequences.[65-67] Although defective poliovirus particles that may be harbored in remaining anterior horn cells during many years of stability appear to become antigenic when ultimately released as these cells degenerate, there is no direct evidence for reactivation of virulent poliovirus in these patients.

Pathogenesis of fatigue. The cause of fatigue in patients with PPS appears to be multifactorial, involving both central and peripheral nervous system mechanisms. Reduced cortical drive to lower motor neurons[68] may play a role in the development of early central fatigue in patients with PPMA. In the periphery, neuromuscular fatigue has been attributed to retraction of axonal sprouts resulting from dying anterior horn cells, as suggested by the presence of increased jitter during single-muscle-fiber electrical recordings, histologic changes of neuromuscular synapses of affected muscles, and the transient amelioration of fatigue in PPMA patients treated with anticholinesterase inhibitors.[69,70] However, no neuromuscular transmission defect in PPMA patients was confirmed in assessment of functional performance and energy utilization of muscles during low-intensity aerobic exercise; rather, it appears that neuromuscular fatigue lies at a point beyond muscle fiber membrane excitation.[71] Histologic abnormalities of oxidative energy metabolism have been shown in clinically affected or asymptomatic muscles of PPMA patients. In addition, during graded aerobic exercise, patients with PPMA showed earlier development of fatigue in clinically unaffected muscles, resulting from impaired oxidative metabolism; patients required a greater dependence on glycolytic energy pathways, as earlier development of intracellular metabolic acidosis rapidly depleted their energy stores of phosphocreatine.[72]

Evaluation of Patients

There are no laboratory parameters that specifically confirm the presence of PPS, and as such, this diagnosis is based on clinical grounds after other medical, orthopedic, neurologic, and psychiatric diseases have been excluded (Table I). Evidence of progression of weakness may be derived from annual evaluations[25] of strength of affected muscle groups. Quantitative isometric or dynamic studies of muscle strength are superior to Medical Research Council manual muscle testing in assessing changes in strength over time. Swallowing studies may provide evidence of progressive bulbar impairment. Serial evaluations of photographs may reveal changes in muscle girth, while muscle size may be studied sequentially with computer tomographic or magnetic resonance imaging techniques.

There are no laboratory parameters that specifically confirm the presence of PPS.

Routine blood tests are usually normal, although muscle creatine kinase may be elevated to 1000 IU/L in up to 10% of patients with PPMA.[24,66] Elevation in cerebrospinal fluid protein without pleocytosis may be observed occasionally.[18] A small percentage of individuals with PPMA demonstrate high IgM antibody titers to poliovirus in serum,[63] as well as elevations of IgM oligoclonal bands specific to poliovirus intrathecally.[64]

Electrodiagnostic evaluations of muscle do not distinguish between residual paralytic poliomyelitis and new symptoms of weakness and atrophy of PPS, but these tests may confirm previous paralytic poliomyelitis in an otherwise unsubstantiated case.[42,49-51] Muscles that were either clinically affected or asymptomatic during the acute phase of polio, and those experiencing new symptoms, may display evidence of abnormal spontaneous activity; this activity appears in the form of fibrillations and positive waves, and abnormally large motor units indicative of remodelling of remaining motor units. Both of these features are indistinguishable from those in patients with previous polio or other neurogenic processes. Similarly, findings of single–motor-unit, single–muscle-fiber, and repetitive-stimulation studies cannot distinguish unequivocally between stable residual polio and PPMA. Nevertheless, these studies do confirm the presence of acute and chronic denervation, and they may be useful to exclude compression neuropathies involving peripheral nerves of the upper and lower extremities, which result from long-standing musculoskeletal deformities or other unrelated neurogenic processes.

While histologic evaluations are not diagnostic of PPS, they may provide evidence of prior polio and support the presence of ongoing neuromuscular remodelling. Neurogenic and myopathic changes are found to varying degrees in biopsied muscles that were previously weakened or unaffected during acute poliomyelitis, and are stable or are now developing new weakness. These changes include large fiber type grouping; groups of atrophic fibers; small, scattered angulated fibers; increased connective tissue; variation of fiber size; and occasional necrotic fibers.[19,24]

Differential diagnosis. The diag-

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oblems, and joint pain. (See ble III for treatment summary, d box, "Resources for PPS Treatnt and Support.")

Muscular weakness. Several studindicate that muscle weakness patients with PPMA may imove significantly with strength ining.[80-82] This remains a central ue in neurorehabilitation[83] beuse earlier uncontrolled studies ggested that excessive exercise patients with reduced innervan could lead to further dame.[84,85] Nevertheless, it was demstrated recently that patients th PPMA who completed a 10eek nonfatiguing, progressiveistance, strength-training proam significantly increased their ength in both symptomatic and nically unaffected muscles—thout serologic or histologic idence of muscle damage.[80] ength was maintained in nearly muscles up to 5 months after cestion of training. The additional nefits of decreasing total fat ass[86] while enhancing bone minal density[87] with strength training ggest that a program of supersed, nonfatiguing, progressive eight-training may be an efficaous therapeutic modality in pants with PPMA.

The swallowing difficulties enuntered by patients with PPMA ay be alleviated by postural adstments, such as dropping the in or turning the head to one side minimize the deficit of a unilatally weakened pharynx.[30] These odifications are best instituted by speech therapist with special aining in dysphagia.

General fatigue. The generalized tigue experienced by most paents with PPS is alleviated to a eat extent with frequent periods rest, lasting between 15 minutes nd 2 hours, after which they are ble to resume their activities.[26] linical studies using prednisone, amantadine, recombinant insulin-like growth factor-1, or alpha-2 recombinant interferon have not demonstrated any consistent improvement in levels of fatigue in patients with PPS, although in individual cases some benefit may be obtained.[88,89] Preliminary study indicates that a component of peripheral neuromuscular fatigue in a small group of PPS patients may be ameliorated with anticholines-

Table III
Treatment of the Post-Polio Syndrome

Post-polio progressive muscular atrophy (PPMA)
- Progressive-resistance, strength-training program for 10 weeks.
- For dysphagia: Speech therapists can help PPMA patients improve swallowing by teaching them postural adjustments, such as dropping the chin or turning the head to one side, to compensate for a unilaterally weakened pharynx.
- Pyridostigmine may be useful for neuromuscular fatigue.

General fatigue
- Frequent periods of rest lasting from 15 minutes to 2 hours.
- Treatment with prednisone, amantadine, insulin-like growth factor-1, or alpha-2 recombinant interferon has not resulted in consistent improvement of fatigue symptoms.

Respiratory or cardiovascular problems
- Aerobic exercise training can significantly enhance oxygen uptake and cardiovascular endurance. Walking on a treadmill, riding a stationary bicycle, and swimming or other pool exercises increase aerobic capacity.

Muscle and joint pain and instability
- Joint pain: analgesics, anti-inflammatory agents, and physical therapy. Gait training, changes in posture, weight reduction, and adjustments to orthotic devices (wheelchair, crutches, orthoses) also improve symptoms. Rarely, surgical repair of unstable joints may be required.
- Aerobic activity also reduces total body fat and improves movement efficiency and activities of daily living.

Resources for PPS Treatment and Support

Post-Polio Syndrome Research Center, NYU Rehabilitation Center
New York University Medical Center
400 E 34th Street, New York, NY 10016
(212) 263-7300

Post-Polio Rehabilitation and Research Service
Kessler Institute for Rehabilitation
300 Market Street, Saddle Brook, NJ 07663-5309
(201) 587-8500

International Polio Network
5100 Oakland Avenue, #206, St. Louis, MO 63110
(314) 534-0475

Polio Survivors Association
12720 La Reina Avenue, Downey, CA 90242
(310) 862-4508

National Center for Medical Rehabilitation Research
National Institutes of Health
Department of Health and Human Services
Executive Plaza South, Room 450 West, 6120 Executive Boulevard
Rockville, MD 20885
(301) 402-2242

terases such as pyridostigmine.[91] A clinical trial studying these agents in a large population of PPS patients with fatigue is ongoing.

Cardiovascular and respiratory problems. Reduced cardiopulmonary function and capacity for oxygen by metabolically impaired muscles may lead to diminished endurance in patients with PPS.[91,92] All ambulatory patients with PPS should consider aerobic exercise training, which, in addition to significantly enhancing oxygen uptake and cardiovascular endurance,[33,93] also reduces total body fat and improves movement efficiency and activities of daily living.[94] Aerobic capacity can be increased by walking on a treadmill, riding a stationary bicycle, or swimming and participating in other pool exercises.

Joint problems. The management of the wide range of musculoskeletal symptoms of PPS patients has depended on supportive care and symptomatic treatment. Joint pain is treated with analgesics, anti-inflammatory agents, and physical therapy. It is not uncommon to encounter patients with new joint pain whose symptoms are improved significantly with gait training, changes in posture, weight reduction, and adjustments to orthotic devices (wheelchair, crutches, orthoses).[95] Rarely, surgical reconstruction may be necessary to repair unstable joints.[96]

New clinical trials. Although no treatment is yet available to reverse the ongoing loss of anterior horn cells and their sprouts in patients with PPMA, clinical trials utilizing neurotrophic factors to stimulate nerve growth are underway. For example, in a study of developing rats, ciliary-derived neurotrophic factor was shown to attenuate the loss of motor neurons that occurs naturally during prenatal development[97] and also spares facial motor neurons in a mouse model of progressive motor neuronopathy.[98] Insulin-like nerve growth factor (IGF-1), a peptide synthesized in muscle, liver, and kidney in response to pituitary growth hormone, has been shown to stimulate anterior horn cells, in vitro and in experimental animals, to generate new axonal sprouts and synapses to muscle fibers.[99] Given that the primary problem in patients with PPMA is the progressive deterioration of remaining motor neurons, these proteins may have the clinical potential to maintain existing motor neurons and their connections. It is possible that such proteins could even stimulate the growth of new nerve terminals (sprouts) to form new synapses, in order to attenuate or reverse the progression of many of the debilitating neuromuscular symptoms of patients with PPMA.

Summary and Conclusions

Of the estimated 1.63 million polio survivors in the US, half may develop PPS.[23] Onset of PPS and the characteristic muscular atrophy typically occurs 10 to 40 years after an initial attack of paralytic polio. Common symptoms include new muscular weakness, pain, and atrophy; dysphagia; respiratory insufficiency including sleep apnea; fatigue; and joint pain and arthritic changes. Exhaustion of remaining motor neurons and loss of innervation of previously asymptomatic muscles appear to be the primary cause of PPS, but immune dysregulation or persistence of chronic polio infection may be contributory. Although PPS is managed primarily by supportive and symptomatic care, nonfatiguing strengthening exercise may result in short-term improvements, and studies are under way to determine whether nerve-growth–stimulating factors may preserve existing motor neurons and their

onnections to muscle. In addition o physical therapy, patients may enefit from psychological counseling as they learn to cope with this isabling and belated aftermath of neir acute poliomyelitis. □

Drugs Mentioned in This Article

Amantadine	*Symmetrel*
Prednisone	Generic
Pyridostigmine	*Mestinon, Regonol*

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